Recent opioid use and fall-related injury among older patients with trauma

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ABSTRACT

BACKGROUND: Evidence for an association between opioid use and risk of falls or fractures in older adults is inconsistent. We examine the association between recent opioid use and the risk, as well as the clinical outcomes, of fall-related injuries in a large trauma population of older adults.

METHODS: In a retrospective, observational, multicentre cohort study conducted on registry data, we included all patients aged 65 years and older who were admitted (hospital stay > 2 d) for injury in 57 trauma centres in the province of Quebec, Canada, between 2004

and 2014. We looked at opioid prescriptions filled in the 2 weeks preceding the trauma in patients who sustained a fall, compared with those who sustained an injury through another mechanism.

RESULTS: A total of 67929 patients were retained for analysis. Mean age was $80.9~(\pm~8.0)$ years and 69% were women. The percentage of patients who had filled an opioid prescription in the 2 weeks preceding an injury was 4.9%~(95%~confidence~interval~[CI]~4.7%-5.1%) for patients who had had a fall, compared with 1.5%~(95%~CI~1.2%-1.8%) for those

who had had an injury through another mechanism. After we controlled for confounding variables, patients who had filled an opioid prescription within 2 weeks before injury were 2.4 times more likely to have a fall rather than any other type of injury. For patients who had a fall-related injury, those who used opioids were at increased risk of in-hospital death (odds ratio 1.58; 95% CI 1.34–1.86).

INTERPRETATION: Recent opioid use is associated with an increased risk of fall and an increased likelihood of death in older adults.

he rate of opioid prescription for pain treatment has been increasing rapidly in North America in the past 20 years. ^{1,2} For example, between 2001 and 2010, the percentage of patients receiving an opioid prescription during an emergency department visit increased from 20.8% to 31%, a relative increase of 49%. ¹ Furthermore, the frequency of opioid prescription increases with age. ³

Opioids are sometimes necessary to treat acute pain, but they can cause adverse effects, especially in the older population.⁴⁻⁶ It has been found that drugs that affect the central nervous system (e.g., drugs that cause sedation and dizziness) can increase the risk of falling.⁷ Falls are frequent among people aged 65 years and older (28%–35% fall each year)⁸ and constitute a leading cause of injuries, hospital admissions and deaths among older people.⁹

Several studies have established an association between opioid use and risk of falls or fractures in the older population. ¹⁰⁻¹⁷ In a nested case–control study, Moden and colleagues found that using psychotropic drugs increased the risk of falls in older people. Specifically, opioid use was more likely to induce a fall within

the next week (odds ratio [OR] = 6.07 for men and 5.16 for women). In another study in a level-1 trauma centre with patients of all ages, falls were more prevalent among patients who had used opioids in the month preceding the trauma compared with patients who had not (32.8% v. 22.0%). Furthermore, Söderberg and colleagues found that taking opioids increases the likelihood of an imminent fall-related injury. For example, having a prescription of opioids filled 1 week before the fall is associated with an OR of 5.14 of falling compared with an OR of 1.23 when the prescription is filled within 4 weeks of the fall. However, other studies did not find a significant association between opioid use and falls, and none examined this in severely injured older people who are at higher risk of death.

The objectives of the study were to examine the association between recent opioid use and the risk, as well as the clinical outcomes, of fall-related injury in a large trauma population of older adults. We hypothesized that fall-related injuries will be more likely to occur with recent opioid use than injuries that occur from other mechanisms.

Methods

Study design and population

We conducted a retrospective, multicentre cohort study using medical consultations and medications from 2 governmental population databases (Quebec Trauma Registry and Régie de l'assurance maladie du Québec [RAMQ]). We included patients aged 65 years and older who were admitted for injury in any of the 57 adult trauma centres (3 level I, 5 level II, 21 level III and 28 level IV) in the province of Quebec, Canada, between Jan. 1, 2004, and Mar. 31, 2014. We excluded patients who were not covered by the RAMQ medication insurance for the year preceding the trauma and patients with no recorded mechanism of their injury.

Data sources

The Quebec Trauma Registry was developed in 1993 and involves the mandatory collection of prospective data for patients admitted to any trauma centre according to the following criteria: deaths following injury, hospital stay greater than 2 days, intensive care unit or transfer from another hospital. Medical archivists extract registry data from patients' medical files using standardized coding protocols. Anatomic injuries are coded with the Abbreviated Injury Scale according to recommendations published by the Association for the Advancement of Automotive Medicine.²¹ The registry is centralized at the RAMQ of the Quebec Ministry of Health and is subject to periodic validation.

The RAMQ medical consultations and medication database is an administrative database maintained by the Quebec Ministry of Health and contains diagnostic information of all medical consultations and medication prescriptions filled for every patient covered by the RAMQ medication insurance in the province of Quebec, which represents 78% of our sample. The medication database contains the date of dispensation, common drug denominations, form, dosage and quantity prescribed by physicians.

We linked the 2 databases using unique anonymous identification numbers provided by the RAMQ. Patient information was available for the time period ranging from 1 year before the trauma to 8 years after hospital discharge (maximum allowed).

Outcomes

We searched for filled opioid prescriptions, including codeine, hydromorphone, meperidine, oxycodone, methadone, fentanyl, tramadol, tramacet, pentazocine and morphine. Hydrocodone is not used for pain management in Canada. Recent opioid use was defined as filling at least 1 opioid prescription during the 14 days preceding the target trauma. To Some authors chose a 28- to 30-day period before trauma, but Söderberg and colleagues found a greater association between opioid use and falls with a 2-week period. In a sensitivity analysis, we divided the recent opioid users into 2 groups: those who used opioids in the 2-week period preceding the trauma but had not filled a prescription for opioids in the previous 3 months (naive opioid user), and those who had used opioids in the 2-week period preceding the trauma and in the previous 3 months (non-naive opioid user).

Variables

From the 2 databases, we extracted the following data: age, sex, injury mechanisms (fall, motor vehicle crash, penetrating injury or blunt object injury), Injury Severity Score (ISS), Abbreviated Injury Scale, number of injuries, duration of stay in emergency department, duration of stay in hospital, surgery during hospital stay and admission to intensive care unit (ICU), as well as history of alcoholism, depression or anxiety 1 year before the target injury. We used an ISS score greater than 15 to define major trauma or polytrauma.²² We used the first digit of the Abbreviated Injury Scale score to identify the injury regions for each wound, and the RAMQ medical consultation database to identify patients who had an International Classification of Disease (ICD)-9 or ICD-10 code for depression, anxiety, alcoholism, falls leading to hospital admission, diagnosis of malignant tumour or other comorbidities (asthma, diabetes, high blood pressure, Parkinson disease, chronic airway obstruction, renal failure, heart failure, coronary artery atherosclerosis and dementia) during the year preceding the injury. Finally, we searched in the RAMQ medication database for at least 1 filled prescription of medication known to affect balance according to the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults²³ (antidepressant, antipsychotic, benzodiazepine, anticholinergic, antithrombotic and cardiovascular drugs) during the 14 days preceding the target trauma.

Statistical analysis

We compared the characteristics of the included sample and those of patients who were excluded using Cohen's effect sizes. We evaluated associations between mechanism of injury (fall v. other) and recent opioid use and clinical characteristics using univariate and multivariate logistic regression analyses.

In patients who had sustained injuries after a fall, we evaluated associations between opioid prescriptions filled 2 weeks before the fall and trauma outcomes using univariate and multivariate logistic regression analyses. Finally, we used a multivariate logistic regression to estimate the association between inhospital mortality and opioid consumption within 2 weeks before the fall while controlling for confounding factors. Finally, as a sensitivity analysis, we evaluated the association between opioid use (naive or non-naive opioid users) and injury mechanism or in-hospital mortality using multivariate logistic regression analyses. Alpha levels were set at 0.05 and all analyses were performed using SPSS version 23 (IBM, Somers, NY).

Ethics approval

Access to the administrative database and medication database maintained by the Quebec Ministry of Health required the approval of the ethics review boards of the Commission d'accès à l'information du Québec and of the Responsable de l'accès à l'information et de la protection des renseignements personnels de la RAMQ.

Results

The Quebec Trauma Registry included a total of 84 241 adult patients aged 65 and older who were admitted for a trauma between 2004 and 2014. Of these patients, we excluded 16.5% because they were not covered by the RAMQ medication insurance

and another 2.8% because they did not have a valid code for injury mechanism, leaving 67929 patients for the final sample (Appendix 1, Supplemental Figure S1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.171286/-/DC1). Excluded patients were similar in all aspects to the selected sample (Appendix 2, Supplemental Table S2, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.171286/-/DC1).

For the whole sample, the mean age was 81.0 (± 8.0) years and 69% were female. The most common mechanism of injury was falls (92%), 59% had surgery and the median hospital stay duration was 12 days. The percentage of patients who had filled an opioid prescription within 2 weeks preceding any type of injury was 4.6% (95% confidence interval [CI] 4.4%–5.0%). This percentage was 4.9% (95% CI 4.7%–5.1%) for patients who had a fall-related injury, and 1.5% (95% CI 1.2%–1.8%) for patients who

had an injury via another mechanism. Opioid prescriptions filled before injuries were most frequently hydromorphone (35%), oxycodone (24%), morphine (20%) and fentanyl (14%).

Table 1 shows the unadjusted and adjusted ORs for patients who had a fall compared with patients who had an injury via another mechanism. Controlling for confounding variables, being older (≥ 85 yr: OR = 5.6; 95% CI 5.1–6.2), being a female (OR = 2.4; 95% CI 2.3–2.5), having filled a prescription of medications known to affect balance (OR = 1.8; 95% CI 1.7–1.9), having falls leading to hospital admissions, having a history of alcoholism during the year before target injury, having a history of fractures, receiving a diagnosis of malignant tumour in the year before the injury, having more comorbidities in the year before the injury, and filling an opioid prescription (within 2 weeks before the injury) were all significantly associated with falls.

	Fall, no. (%)*	Other, no. (%)*†	Unadjusted	Adjusted‡
Predictors	n = 62 284	n = 5645	OR (95% CI)	OR (95% CI)
Sex				
Female	44 108 (70.8)	2535 (44.9)	2.98 (2.82-3.15)	2.40 (2.27-2.54)
Male	18 176 (29.9)	3110 (55.1)	Reference	Reference
Age category, yr				
65–74	14 357 (23.1)	2823 (50.0)	Reference	Reference
75–84	25 790 (41.4)	2205 (39.1)	2.30 (2.17-2.44)	2.00 (1.88-2.13)
≥ 85	22 137 (35.5)	617 (10.9)	7.06 (6.45–7.72)	5.63 (5.14-6.16)
History of alcoholism				
Yes	750 (1.2)	69 (1.2)	0.99 (0.78-1.26)	1.63 (1.26-2.10)
No	61 534 (98.8)	5576 (98.8)	Reference	Reference
Prescription of medications§ known to	o affect balance filled	2 wk before injury		
Yes	19 111 (30.7)	951 (16.8)	2.19 (2.03-2.35)	1.80 (1.67–1.94)
No	43 173 (69.3)	4694 (83.2)	Reference	Reference
Falls leading to hospital admission in y	r before injury			
Yes (≥ 1)¶	1230 (2.0)	38 (0.7)	2.97 (2.15-4.11)	1.77 (1.27–2.48)
No	61 054 (98.0)	5607 (99.3)	Reference	Reference
Fractures in yr before injury				
Yes	4359 (7.0)	224 (4.0)	1.82 (1.59–2.09)	1.38 (1.20-1.59)
No	57 925 (93.0)	5421 (96.0)	Reference	Reference
Diagnosis of malignant tumour in yr b	efore injury			
Yes	8946 (14.4)	813 (14.4)	1.00 (0.92-1.08)	1.10 (1.01-1.19)
No	53 338 (85.6)	4832 (85.6)	Reference	Reference
No. of comorbidities, mean ± SD	0.77 ± 0.84	0.68 ± 0.80	1.14 (1.10-1.18)	1.09 (1.05–1.13)
Opioid prescription filled within 2 wk l	pefore injury			
Yes	3041 (4.9)	85 (1.5)	3.36 (2.70-4.17)	2.42 (1.94-3.02)
No	59 243 (95.1)	5560 (98.5)	Reference	Reference

Note: CI = confidence interval, OR = odds ratio; SD = standard deviation.

^{*}Unless otherwise indicated.

[†]ORs are presented for falls compared with motor vehicle crash and weapons or penetrating injury mechanisms. ‡Adjusted for all variables included in this table.

[§]Antidepressant, antipsychotic, benzodiazepine, anticholinergic, antithrombotic and cardiovascular drugs.

[¶]Only 0.2% had 2 or more falls leading to hospital admission in the year before the target injury.

Notably, patients who had filled an opioid prescription within 2 weeks before injury were 2.4 times (95% CI 1.9–3.0) more likely to have suffered a fall rather than an injury via another mechanism.

For patients who had suffered a fall-related injury, those who had filled an opioid prescription within 2 weeks before the injury had significantly more thorax and spine regions affected, were more likely to

be women and had longer hospital stays (Table 2). There was also an increase in mortality during hospital stay in these patients compared with those who did not use opioids. However, recent opioid use was associated with a decreased number of ICU admissions, a decreased need for surgery, a decreased number of incidents of major trauma (ISS > 15), a decreased number of patients with 3 injuries or more and

	Opioid u	se, n (%)†		
Predictors	Yes n = 3041	No n = 59 243	Unadjusted OR (95% CI)	Adjusted‡ OR (95% CI)
Sex				
Female	2375 (78.1)	41 732 (70.4)	1.50 (1.37-1.64)	1.51 (1.38-1.65)
Male	665 (21.9)	17 511 (29.6)	Reference	Reference
Age category, yr				
65–74	670 (22.)	13 687 (23.1)	Reference	Reference
75-84	1287 (42.3)	24 503 (41.4)	1.07 (0.98-1.18)	0.97 (0.88-1.07)
≥85	1084 (35.6)	21 053 (35.5)	1.05 (0.95-1.16)	0.87 (0.79-1.00)
No. of injuries				
1	1976 (65.0)	37 580 (63.4)	Reference	Reference
2	624 (20.5)	11 747 (19.8)	1.01 (0.92-1.11)	0.97 (0.88-1.07)
≥3	441 (14.5)	9916 (16.7)	0.85 (0.76-0.94)	0.84 (0.73-0.97)
AIS injury regions				
Head	355 (11.7)	8690 (14.7)	0.77 (0.69-0.86)	0.97 (0.87-1.13)
Face	243 (8.0)	5596 (9.4)	0.83 (0.73-0.95)	0.92 (0.79-1.07)
Neck	8 (0.3)	187 (0.3)	0.83 (0.41-1.69)	0.89 (0.44-1.83)
Thorax	444 (14.6)	7203 (12.2)	1.24 (1.11–1.37)	1.29 (1.15–1.44)
Abdomen	44 (1.4)	1170 (2.0)	0.73 (0.54-1.00)	0.72 (0.53-1.00)
Spine	399 (13.1)	6508 (11.0)	1.22 (1.10-1.36)	1.19 (1.05–1.34)
Upper extremity	716 (23.5)	14 471 (24.4)	0.95 (0.87-1.04)	1.91 (0.91-1.12)
Lower extremity	2106 (69.3)	40 537 (68.4)	1.04 (0.96-1.13)	1.11 (1.00-1.22)
Major trauma (ISS > 15)				
Yes	199 (6.5)	5678 (9.6)	0.66 (0.57-0.77)	0.76 (0.63-0.92)
No	2842 (93.5)	53 565 (90.4)	Reference	Reference
Surgery during hospital st	ay			
Yes	1626 (53.5)	35 503 (59.9)	0.77 (0.71-0.83)	0.74 (0.68-0.80)
No	1415 (46.4)	23 740 (40.1)	Reference	Reference
Admission to intensive ca	re unit			
Yes	259 (8.5)	5874 (9.9)	0.85 (0.74-0.96)	0.94 (0.82-1.08)
No	2782 (91.5)	53 369 (90.1)	Reference	Reference
Death at hospital				
Yes	174 (5.7)	2331 (3.9)	1.48 (1.27-1.74)	1.58 (1.34-1.86)
No	2867 (94.3)	56 912 (96.1)	Reference	Reference
Median (IQR) hospital stay duration (d)	14 (18)	12 (16)	1.04 (1.03–1.06)§	1.04 (1.03–1.06)

Note: AIS = Abbreviated Injury Scale, CI = confidence interval, IQR = interquartile range, ISS = Injury Severity Scale, OR = odds ratio.

^{*}Associations between opioid use within 2 weeks before the injury and trauma outcomes for patients who had a fall as injury mechanism (n = 62 284). †Unless otherwise indicated.

[‡]Adjusted for all variables included in the table.

[§]OR is expressed for each 10 days.

a decreased number of head and face injuries. When controlled for all other variables, the variables of ICU admission and head or face injuries were no longer statistically significant.

Controlling for confounding factors, patients who filled an opioid prescription within 2 weeks before falling were at increased risk (OR = 1.59; 95% CI 1.35-1.87) of death during their hospital stay. Being male, being older, presenting with major trauma, being admitted to the ICU, having multiple comorbidities, having filled a prescription of antipsychotics within 14 days before the injury and having a malignant tumour in the year

Table 3: Predictors associated with death in hospital for patients with fall as the
injury mechanism*

	Hospital mort	tality, no. (%)†	
Predictors	Yes n = 2505	No n = 59 779	Adjusted OR† (95% CI)
Sex			
Male	1020 (40.7)	17 156 (28.7)	1.58 (1.45-1.73)
Female	1485 (59.3)	42 623 (71.3)	Reference
Age category, yr			
65-84	283 (11.3)	14 073 (23.5)	Reference
75–84	895 (35.7)	24 895 (41.6)	2.05 (1.79–2.36)
≥ 85	1326 (52.9)	20 811 (34.8)	4.41 (3.83-5.05)
No. of injuries			
1	1454 (58.0)	38 102 (63.7)	Reference
2	474 (18.9)	11 897 (19.9)	1.02 (0.92–1.14)
≥3	577 (23.0)	9780 (16.4)	1.13 (1.01–1.27)
Major trauma (ISS > 15)			
Yes	506 (20.2)	5371 (9.0)	1.65 (1.46-1.86)
No	1999 (79.8)	54 408 (91.0)	Reference
Admission to intensive care	unit		
Yes	747 (29.8)	5386 (9.0)	4.05 (3.67-4.47)
No	1758 (70.2)	54 393 (91.0)	Reference
Diagnosis of malignant tum	our in yr before fall		
Yes	459 (18.3)	8487 (14.2)	1.28 (1.15-1.42)
No	2046 (81.7)	51 292 (85.8)	Reference
No. of comorbidities, mean ± SD	0.86 ± 0.90	0.77 ± 0.83	1.07 (1.03–1.13)
Antidepressant prescription	filled within 2 wk b	efore fall	
Yes	493 (19.7)	11 635 (19.5)	0.96 (0.86-1.07)
No	2012 (80.3)	48 144 (80.5)	Reference
Antipsychotic prescription fi	illed within 2 wk be	fore fall	
Yes	306 (12.2)	4731 (7.9)	1.77 (1.55–2.01)
No	2199 (87.8)	55 048 (92.1)	Reference
Benzodiazepine prescription	n filled within 2 wk I	before fall	
Yes	57 (2.3)	1577 (2.6)	0.89 (0.68-1.17)
No	2448 (97.7)	58 202 (97.4)	Reference
Opioid prescription filled wi	thin 2 wk before fal	l	
Yes	174 (6.9)	2867 (4.8)	1.59 (1.35–1.87)

Note: CI = confidence interval, ISS = Injury Severity Scale, OR = odds ratio, SD = standard deviation. *Patients who had a fall as injury mechanism: $n = 62\ 284$.

[†]Unless otherwise indicated.

[‡]Adjusted for all variables included in the table.

before the fall were also significantly associated with in-hospital mortality (Table 3).

In a sensitivity analysis, naive (adjusted OR = 2.25; 95% CI 1.61-3.15) and non-naive (adjusted OR = 4.17; 95% CI 3.14-5.54) opioid users had an increased risk of falls compared with another mechanism of injury. There was also an increase in mortality during hospital stay in naive (adjusted OR = 1.70; 95% CI 1.28-2.27) and non-naive (adjusted OR = 1.54; 95% CI 1.27-1.87) opioid users compared with those who did not use opioids.

Interpretation

This study confirms an association between recent opioid use and fall-related injury in a large trauma population of older adults (67 929 patients). Furthermore, it shows that pre-injury opioid use is also associated with increased hospital mortality for older patients with a fall-related injury. Patients included in the registry had a median hospital stay of 14 days and had to undergo surgery in more than 50% of cases, suggesting that these injuries had serious consequences. Results were similar for opioid-naive or non-opioid-naive older trauma patients.

Concordant with our results, opioid use has been previously associated with increased risk of fall-related injury. 10-14,16,17 Our OR of 2.4 (when adjusted for confounders) is comparable with that observed in other studies based on older populations: hazard ratio (HR) of 2.05 in hip fractures, 17 OR of 3.3 for fall or fracture, 11 HR of 2.27 for injury with codeine combination, 16 and HR of 4.9 for any fractures. 14 Adverse effects, like the sedation and dizziness frequently observed with opioids, 24 can compromise coordination and be responsible for fall-related injuries, especially in the older population with increased visual impairment and loss of balance. 13 In addition to previous opioid use, being a female, being older, having a history of alcoholism and using antidepressants or antipsychotics drugs were significantly associated with fall-related injuries, which is in accordance with previous studies. 13,15,25-27

We found that more women than men had filled an opioid prescription before the fall-related injury. Another study found the same result but for all types of injury mechanisms. This suggests that women could be more susceptible to the adverse effects of opioids. ¹⁰ There was also a significant but weak association between opioid use before the trauma and back or thoracic injury. This could suggest that older patients who are taking opioids are less inclined to slow down their fall with their arms.

Patients with fall-related injury and recently filled opioid prescriptions had less major trauma, fewer surgeries and fewer concurrent injuries than patients who did not use opioids before the fall, suggesting that their injuries were potentially less severe. However, their median hospital stay was longer and they died more often during the hospital stay, suggesting that a fall associated with opioid use may be a marker of frailty. The only other study that examines mortality with opioid use in trauma patients found no significant relation between the two.¹⁰ However, the mean age of that sample was younger (42 yr) and included all types of injury mechanisms. It is possible that older patients could be more vulnerable to opioid use than younger patients and, as stated before, it is likely that a fall associated with opioid use is a marker of frailty.

Because these results were not the primary outcome of the present study, they should be confirmed by future studies.

Limitations

This study has some limitations. The retrospective design of the study can demonstrate only an association between opioid use and falls; no causal relationship between the two phenomena can be inferred. We can hypothesize that because patients generally use opioids to treat pain, it may be the pain itself (and not the opioid) that causes the fall. Furthermore, our definition of opioid use is filling an opioid prescription in the previous 2 weeks, and it is possible that the drug was not consumed by the patient. However, this is also true for patients with other mechanisms of injury. Medications administered during the target hospital stay were not available and therefore could not be controlled in the mortality analysis. In addition, our fall-related injury group was compared with a group of older patients who had other mechanisms of injury (motor vehicle crash or penetrating trauma). These latter patients could have some characteristics that differed from a group of older patients who did not have injury. However, opioids can also affect the attention and reaction time of drivers, so opioid use could also have been a factor for patients who had motor crashes.²⁸ Consequently, our association between opioid use and falls could have been higher. Furthermore, we studied only falls that were related to substantial injuries and led to a hospital stay, so the frequency of fall associated with opioids could be higher. Examining only falls related to substantial injuries could also explain the association that we found between opioids and increased in-hospital mortality. Finally, as stated earlier, falls associated with opioid use could be a marker of frailty and not necessarily point to a causal association.

Physicians should be aware that prescribing opioids to older adults is not only associated with an increased risk of falls but also, if these patients do fall, a higher in-hospital mortality rate.

Conclusion

These results show that recent opioid use is associated with an increased risk of falls in older adults and an increased likelihood of death in those with fall-related injuries.

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